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APPLICANT(S):	Farmer, <i>et al.</i>	CONFIRMATION NO.	5510
SERIAL NO.:	10/581,781	EXAMINER:	Irene Marx
FILING DATE:	April 12, 2007	ART UNIT:	1651
TITLE:	METHODS FOR THE DIETARY MANAGEMENT OF IRRITABLE BOWEL SYNDROME AND CARBOHYDRATE MALABSORPTION		

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO JANUARY 12, 2009 OFFICE ACTION

This paper is in response to the January 12, 2009 Office Action. Applicants submit herewith a Petition for a Three-Month Extension of Time, along with the appropriate fee. With the three-month extension, these documents are due on or before July 13, 2009 (July 12, 2009 being a Sunday).

Applicants believe no additional fees are due. However, the Commissioner is hereby authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 19374-515 NATL.

Amendments to the Specification begin on page 2.

Amendments to the Claims begin on page 3.

Remarks begin on page 4 of this paper.

Inventor(s): Farmer, *et al.*
Serial No.: 10/581,781

Amendments to the Specification:

Please amend the Title of the Invention on page 1, line 1 as follows:

Methods for Increasing Lactose Digestion ~~the dietary management of irritable bowel syndrome and carbohydrate malabsorption~~

Please amend the following paragraphs beginning on page 1, after the Title of the Invention as follows:

RELATED APPLICATIONS

This application is a national stage application, filed under 35 U.S.C. §371, of International Application No. PCT/US2004/040513, filed on December 3, 2004 ~~February 23, 2005~~, which claims the benefit of U.S.S.N. 60/528,074, ~~filed December 5, 2003~~ and U.S.S.N. 10/915,030, filed August 9, 2004, which claims the benefit of 60/528,074, filed December 5, 2003, and is a continuation-in-part of U.S.S.N. 09/369,016, filed August 5, 1999, which claims the benefit of 60/095,786, filed August 7, 1998, each ~~both~~ of which are incorporated herein by reference in their entirety.

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1-52. (Canceled).

53-58. (Canceled).

59. (Currently amended). A method for increasing lactose digestion in a subject, comprising the steps of:

identifying a subject patient suffering from or at risk of developing lactose intolerance, and

administering to said subject patient a composition comprising an effective amount of viable *Bacillus coagulans* bacteria and a supplemental lactase, wherein said bacteria is selected from the group consisting of GBI-20 (ATCC Designation Number PTA-6085), GBI-30 (ATCC Designation Number PTA-6086), and GBI-40 (ATCC Designation Number PTA-6087),

whereby lactose digestion in said subject is increased following said administration.

60. (Currently amended). The method of claim 59, wherein the subject patient is human.

61. (Original). The method of claim 59, wherein said lactase is provided in a concentration from about 1000 IU to about 12,000 IU.

62.-76. (Canceled).

77.-79. (Canceled).

REMARKS

Upon entry of this amendment, claims 59-61 are pending in this application. Claims 53-58 and 77-79 have been canceled for being drawn to non-elected invention. Claims 59 and 60 have been amended. Support for the amendment to claim 59 can be found throughout the specification, *e.g.*, at least at page 2, lines 11-17; at page 3, lines 10-13; and at page 4, lines 17-19 of the specification. Applicants have amended the Title of Invention to clearly identify the invention to which the claims are directed, as requested by the Examiner. Applicants have also amended the Related Application Section to correct the priority claim of the instant application. No new matter is added.

Objection to the Title

The Examiner states that a new Title is required that is clearly indicative of the invention to which the claims are directed. *See*, Office Action at page 2. As the claims are directed to methods of increasing lactose digestion, the Title of the Invention has been amended to recite, "Methods for Increasing Lactose Digestion". This objection should be reconsidered and withdrawn.

Double Patenting

Claims 59-61 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-5, 7, 17-20, and 30-32 of co-pending application U.S.S.N. 11/985,617. *See*, Office Action at pages 2-3.

Applicants disagree. However, in the interest of expediting prosecution of the present application, Applicants file herewith a terminal disclaimer in compliance with 37 C.F.R. §1.321(c). Withdrawal of this rejection is respectfully requested.

Rejections Under 35 USC § 103(a)

Claims 59-61 are rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 99/49877 to Farmer taken with U.S. Patent No. 6,410,018 to Eisenhardt ("Eisenhardt"). *See*, Office Action at page 3.

According to the Examiner, WO 99/49877 describes the probiotic effects of *Bacillus coagulans*, and more specifically, a method of administering *Bacillus coagulans* to reduce

cholesterol. The Examiner also states that WO 99/4987 describes the addition of a supplemental lactase to the composition of *Bacillus coagulans*. The Examiner further states that Eisenhardt describes that the administration of a lactase enzyme is useful for increasing lactose digestion. *See*, Office Action at page 3. The Examiner concludes that the claimed invention as a whole was *prima facie* obvious in view of the cited references. *See*, Office Action at page 4.

Independent claim 59, from which the remaining claims depend, has been amended to require a method for increasing lactose digestion in a subject by identifying a subject suffering from or at risk of developing lactose intolerance, and administering to the subject a composition comprising an effective amount of viable *Bacillus coagulans* bacteria and a supplemental lactase, wherein the bacteria is selected from the group consisting of GBI-20 (ATCC Designation Number PTA-6085), GBI-30 (ATCC Designation Number PTA-6086), and GBI-40 (ATCC Designation Number PTA-6087), whereby lactose digestion in the subject is increased following the administration.

First, neither WO 99/49877, nor Eisenhardt describe or suggest the administration of the specific strains of *Bacillus coagulans* required by the claims, *i.e.*, GBI-20 (ATCC Designation Number PTA-6085), GBI-30 (ATCC Designation Number PTA-6086), or GBI-40 (ATCC Designation Number PTA-6087).

Additionally, the notion of the addition of a supplementary enzyme, such as a lactase, appears merely once in the entire description of WO 99/49877, among a more extensive list of optional additional components. Specifically, WO 99/49877 recites that additional components of a therapeutic composition can include assorted colorings or flavorings, vitamins (*e.g.*, vitamins B, C, D, E, folic acid, K, niacin, and the like), enzymes (*e.g.*, lactase, amylase, glucanase, catalase, and the like), and other nutrients. *See*, WO 99/49877 at page 22, lines 1-8.

Applicants respectfully submit that it is an established principle of U.S. patent law that the mere fact that a species is listed among a more extensive list of species does not arise to the level of a motivation to select one specific member from the recited list for use in the featured methodology. M.P.E.P. § 2144.08. In particular, it has been held that rejection of a claimed compound in light of a large prior art genus "is not appropriate where the prior art does not disclose a *small recognizable class of compounds with common properties*." *C.f.*, *In re Ruschig*, 343 F.2d 965, 974, 145 USPQ 274, 282 (CCPA 1965). (Emphasis added).

Applicants respectfully submit that the ordinary skilled artisan would not have been motivated to use the *Bacillus coagulans* and lactase described by WO 99/49877 for increasing lactose digestion, as presently claimed. The mere fact that WO 99/49877 lists "lactase" in a more extensive list of additional components does not rise to the level of a motivation to select one specific member from the recited list of components for use in the claimed method of increasing lactose digestion. In fact, WO 99/49877 does not describe or suggest any methods of increasing lactose digestion in a subject suffering from or at risk of developing lactose intolerance.

Moreover, Applicant respectfully submits that the ordinary skilled artisan would not have been motivated to combine the teachings of WO 99/49877 with those of Eisenhardt to reach the claimed invention with predictable results. Even if the skilled artisan were to rely on WO 99/49877 for describing a method of administering *Bacillus coagulans* for its probiotic effects, he would not have been motivated to combine the teachings with those of Eisenhardt to arrive at the claimed methods of increasing lactose digestion in a subject suffering from or at risk of developing lactose intolerance, as Eisenhardt does not even mention the administration of probiotic bacteria (and certainly not *Bacillus coagulans*) for increasing lactose digestion.

For the foregoing reasons, the claimed methods are non-obvious over the teachings of WO 99/49877 and Eisenhardt either alone or in combination. Accordingly, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Claims 59-61 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Mustapha *et al.*, 1997 J. Dairy Sci., 80: 1537-1545 ("Mustapha"), taken with 6,410,018 to Eisenhardt ("Eisenhardt"), Farmer and Mikhail, 1997 Empower, 5-7 and 42-43, ("Farmer I"), Farmer and Mikhail, 1998 Empower 1(3): 8 and 38-41, ("Farmer II"), and US Patent No. 4,179,335 to Long ("Long"). *See*, Office Action at page 4.

According to the Examiner, Mustapha describes that consumption of *Lactobacillus* increases lactose digestion in patients suffering from or at risk of developing lactose intolerance. *See*, Office Action at page 4. The Examiner states that "it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the process of increasing lactose digestion in people at risk of developing lactose intolerance as taught by Mustapha *et al.* of using a lactase producing strain of the probiotic *Lactobacillus acidophilus* by

substituting therefor a strain of *B. coagulans* (*Lactobacillus sporogenes*) recognized in the art as being a suitable probiotic, resistant to environmental insults in the gastrointestinal tract, as taught by Farmer (I) and Farmer (II) as well as an efficient producer of lactase...". Office Action at page 5. The Examiner concludes that the claimed invention as a whole was *prima facie* obvious in view of the cited references. *See*, Office Action at page 5.

Applicants disagree. However, in the interest of expediting prosecution of the present application, claim 59, from which the remaining claims depend, has been amended to require the administration of *Bacillus coagulans* bacteria selected from the group consisting of GBI-20 (ATCC Designation Number PTA-6085), GBI-30 (ATCC Designation Number PTA-6086), and GBI-40 (ATCC Designation Number PTA-6087).

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. Further, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

First, Applicants submit that the Examiner has not applied the *prima facie* case of obvious standard as required by MPEP § 2143. Applicants submit that Mustapha does not describe or suggest the administration of *Bacillus coagulans* bacteria selected from the group consisting of GBI-20 (ATCC Designation Number PTA-6085), GBI-30 (ATCC Designation Number PTA-6086), and GBI-40 (ATCC Designation Number PTA-6087), as required by independent claim 59, from which the remaining claims depend.

Moreover, there was an error in the early nomenclature of *Bacillus coagulans*, as *Bacillus coagulans* was previously mis-characterized as a *Lactobacillus* and labeled as *Lactobacillus sporogenes*. However, initial classification was incorrect because *Bacillus coagulans* produces spores and excretes L(+)-lactic acid through metabolism. These developmental and metabolic aspects required that the bacterium be reclassified as a lactic acid *Bacillus* to properly and more accurately reflect its phenotype. In addition, it is not generally appreciated that classic *Lactobacillus* species are unsuitable for colonization of the gut due to their instability in the

harsh (*i.e.*, acidic) pH environment of the bile, particularly human bile. By contrast, *Bacillus coagulans* is able to survive and colonize the gastrointestinal tract in the bile environment and even grown in this low pH range. *See*, Specification at page 11, lines 4-13. The claimed strain is not a *Lactobacillus*, but a *Bacillus* - *Bacillus coagulans*. Thus, the Examiner's reasons for rejecting the claims are based on a false suggestion of similarity between members of the *Bacillus* genus and members of the *Lactobacillus* genus of bacteria.

Furthermore, Farmer II reports that *Bacillus coagulans* has many differences from *Lactobacillus* species, such as the ability to form spores and produce L(+) lactic acid, which is completely metabolized into glycogen. By contrast, most *Lactobacillus* species produce D(-) lactic acid, which is metabolized more slowly and can lead to acidosis. *See*, Farmer II at page 41, columns 1-2. Farmer II also states that *Bacillus coagulans* survives stomach acids and other digestive enzymes and moves through the intestines without loss of viability, while *Lactobacillus* species do not survive well in stomach acids and little if any *Lactobacilli* survive to colonize the intestines. *See*, Farmer II at page 41, column 2. Thus, Applicants submit that the claimed *Bacillus coagulans* bacteria is significantly different, indeed provides advantages over, *Lactobacillus* species. Therefore, Applicants submit that contrary to the Examiner's contention, it would not be obvious to substitute *Bacillus coagulans* for the *Lactobacillus acidophilus* of Mustapha to arrive at the claimed invention.

Finally, even among the *Lactobacillus* genus, not all lactase-producing bacteria reduce lactose malabsorption. To the contrary, when examining the ability of a selected few *Lactobacillus acidophilus* strains to reduce lactose malabsorption, Mustapha determined that *Lactobacillus acidophilus* ATCC 4356 did not reduce carbohydrate malabsorption. *See*, Mustapha at Abstract.

Secondary references, Eisenhardt, Farmer I, Farmer II, and Long do not cure the deficiencies of Mustapha, as neither Farmer I, nor Eisenhardt, nor Farmer II, nor Long describe or suggest the administration of the specific strains of *Bacillus coagulans* required by the claims, *i.e.*, GBI-20 (ATCC Designation Number PTA-6085), GBI-30 (ATCC Designation Number PTA-6086), or GBI-40 (ATCC Designation Number PTA-6087).

For the foregoing reasons, the claimed methods are non-obvious over the teachings of Mustapha, Eisenhardt, Farmer I, Farmer II, and Long either alone or in combination. Accordingly, Applicants respectfully request that the rejection of the claims under 35 U.S.C.

Inventor(s): Farmer, *et al.*
Serial No.: 10/581,781

§ 103(a) be reconsidered and withdrawn.

CONCLUSION

On the basis of the foregoing remarks, Applicants respectfully submit that this paper is fully responsive and that the pending claims are in condition for allowance. Such action is respectfully requested. If there are any questions regarding these remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



Ingrid A. Beattie, Reg. No. 42,306
Daniel W. Clarke, Reg. No. 63,993
Attorneys for Applicant
c/o MINTZ LEVIN
Tel.: (617) 542-6000
Fax: (617) 542-2241
Customer No. 30623

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